The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte FRANCIS Y. F. LEE

Appeal 2007-1033
Application 10/091,061
Technology Center 1600

Decided June 19, 2007

Before DEMETRA J. MILLS, ERIC GRIMES, and NANCY J. LINCK, *Administrative Patent Judges*.

Opinion by GRIMES, *Administrative Patent Judge*. Dissenting opinion by LINCK, *Administrative Patent Judge*.

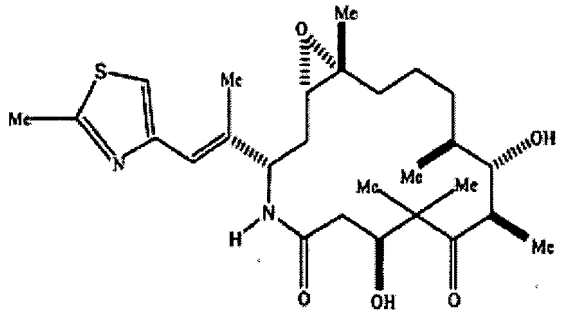
DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of treating cancer. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

The Specification describes a "method for the treatment of anti-proliferative diseases, including cancer, which comprises administering to a mammalian specie in need thereof a synergistically, therapeutically effective

amount of: (1) at least one anti-proliferative agent and (2) a compound of formula I" (Spec. 2-3). A preferred compound of Formula I is Compound 1:



(*id.* at 17). "Suitable anti-proliferative agents . . . include . . . capecitabine" (*id.* at 8-9).

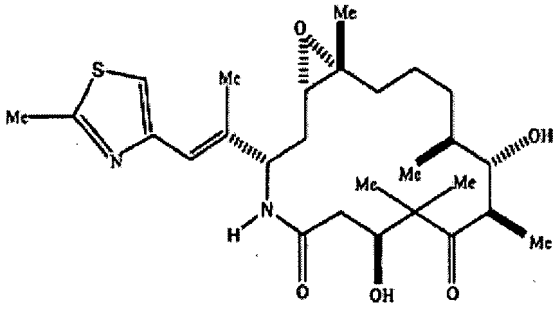
DISCUSSION

1. CLAIMS

Claims 117-130 are on appeal. Claims 101-111 and 113-116 are also pending and rejected, but the rejections of these claims have not been appealed. Thus, the Examiner is entitled to cancel claims 101-111 and 113-116. See MPEP § 1215.03.

We will focus on claim 117, the broadest claim on appeal, which reads:

117. A method of treating cancer in a mammal selected from metastatic breast cancer, lung cancer, pancreatic cancer, ovarian cancer, prostate cancer, colon cancer, and/or small cell lung cancer, comprising administering to the mammal a therapeutically-effective combination of (1) a dosage unit of capecitabine and (2) a dosage unit of Compound (1), having the formula,



or a pharmaceutically-acceptable hydrate, solvate, or geometric, optical, or stereoisomer of Compound (1), wherein the administration will provide a greater anti-cancer effect than the effect obtainable with either the dosage unit of capecitabine or the dosage unit of Compound (1) alone.

Thus, claim 117 is directed to a method of treating one of several specified cancers in a mammal by administering capecitabine and Compound 1. Claim 117 also recites that the combination of capecitabine and Compound 1 provides greater anti-cancer effect than either compound alone.

2. REFERENCES

The Examiner relies on the following references:

Danishefsky	6,867,305 B2	Mar. 15, 2005
Vite	WO 99/02514	Jan. 21, 1999

Miwa, "Design of a Novel Oral Fluoropyrimidine Carbamate, Capecitabine, which Generates 5-Fluorouracil Selectively in Tumours by Enzymes Concentrated in Human Liver and Cancer Tissue," European Journal of Cancer, Vol. 34, No. 8, pp. 1274-1281 (1998)

The Merck Index, Cancer Chemotherapy Drug Regimens, the Merck Index, 12th Edition, pp. Misc-10, (1996)

3. OBVIOUSNESS

Claims 101-111 and 113-130 stand rejected under 35 U.S.C. § 103 as obvious over Vite in view of The Merck Index and Miwa. In addition, claims 102-104 and 117-125 stand rejected under 35 U.S.C. § 103 as obvious over Danishefsky in view of Miwa. Appellant appeals the rejections of claims 117-130.

The Examiner relies on Vite for disclosing that Compound 1 "is useful in treating various types of cancers or tumors" and that this compound

"is useful in combination with known anti-cancer and cytotoxic agents for cancer treatment" (Answer 6).

The Examiner relies on Danishefsky for disclosing that a pharmaceutical composition comprising Compound 1 is useful in methods of treating cancer (*id.* at 3). The Examiner argues that Danishefsky discloses that its compounds can be used in combination with "other cytotoxic agents or anticancer agents such as 5-fluorouracil (5-FU)" (*id.* at 4).

The Examiner relies on The Merck Index for teaching that "fluorouracil (5-FU) is well-known to be used in combination cancer chemotherapy, i.e., comb[in]ing with other anti-cancer agents as cancer chemotherapy drug regimens" (*id.* at 6).

The Examiner relies on Miwa for disclosing that "capecitabine . . . , which is finally converted to 5-fluorouracil (5-FU) by dThdPase in tumors, should be much safer and more effective than 5-FU, for treating cancers or various types of tumors" (*id.* at 4-5, 6).

The Examiner concludes that "[i]t would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ [Compound 1] in combination with . . . capecitabine in . . . a method for treating cancer" (*id.* at 6-7). In particular, the Examiner argues that there would have been motivation to combine the references in this way and there would have been a reasonable expectation of success because Compound 1 "is known to be useful in treating various types of cancers or tumors . . . and also useful in combination with known anti-cancer and cytotoxic agents for cancer treatment," "fluorouracil (5-FU) is well-known to be used in combination cancer chemotherapy," and "[c]apecitabine . . . is known to be

finally [converted] to 5-fluorouracil (5-FU) by dThdPase in tumors, and should be much safer and more effective than 5-FU, for treating cancers or various types of tumors" (*id.* at 7).

We conclude that the Examiner has set forth a prima facie case that it would have been obvious to administer Compound 1 in combination with capecitabine to treat cancer. In particular, we agree with the Examiner that the combination would have been suggested by the known use of various anti-cancer agents in combination. As recently indicated by the Supreme Court, "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007). In addition, we agree with the Examiner that there would have been a reasonable expectation that administering capecitabine in combination with Compound 1 would provide a greater anti-cancer effect than would administering either capecitabine or Compound 1 alone.

Appellant, however, has provided evidence to rebut the Examiner's prima facie case of obviousness. "If a *prima facie* case is made in the first instance, and if the applicant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed." *In re Hedges*, 783 F.2d 1038, 1039, 228 USPQ 685, 686 (Fed. Cir. 1986).

Appellant relies on the Declaration of Francis Lee (submitted October 31. 2005). The Declaration describes experiments in which capecitabine and Compound 1 (referred to in the Declaration as ixabepilone)

were administered to tumor-bearing mice, alone or in combination (Declaration ¶¶ 10-13). The results show that the combination of capecitabine and ixabepilone resulted in slower tumor growth and greater anti-tumor efficacy (*id.* at ¶ 14). Dr. Lee declared that the results "demonstrated [that] a synergistic effect is obtained in preclinical studies involving the administration of ixabepilone and capecitabine, in combination, and that [he] found this effect to be surprising" (*id.* at ¶ 15).

"Synergism, in and of itself, is not conclusive of unobviousness in that synergism might be expected." *In re Kollman*, 595 F.2d 48, 55 n.6, 201 USPQ 193, 198 n.6 (CCPA 1979). "[H]owever, when an applicant demonstrates *substantially* improved results . . . and *states* that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of* evidence to the contrary." *In re Soni*, 54 F.3d 746, 751, 34 USPQ2d 1684, 1688 (Fed. Cir. 1995) (emphases in original).

The Examiner does not dispute that the data in the Declaration show synergism, or that a synergistic effect was unexpected. Rather, the Examiner argues that "the Declaration is not relevant because it is not commensurate with the scope of the claims" (Answer 10). In particular, the Examiner argues that: (a) "the claims are drawn [to] various cancers, of which the Declaration has support for only colon cancer"; (b) "there is only one data point in the Declaration drawn to 10 mg/kg of compound (1) and 250 mg/kg/adm of capecitabine, whereas the claims are drawn to all dosage ranges of both compound (1) and capecitabine"; and (c) "the results of the Declaration clearly provide only a delay in tumor growth, while the claims

are drawn to treating cancer, which is construed as both inhibition and regression of cancer" (*id.*).

We do not agree with the Examiner that the Declaration fails to overcome the prima facie case. First, "commensurate in scope" means that the evidence provides a reasonable basis for concluding that the untested embodiments encompassed by the claims would behave similarly to the tested embodiment(s). *See In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) ("Here, only one mixture of ingredients was tested. . . . The claims, however, are much broader in scope, . . . and we have to agree with the Patent Office that there is no 'adequate basis for reasonably concluding that the great number and variety of compositions included by the claims would behave in the same manner as the [single] tested composition.'") (bracketed material in original).

In this case, the Examiner has not provided any reason why, in view of the Declaration, a synergistic effect would not also be expected for other cancers and at different dosages. In this regard, we note that Vite generally teaches that compounds of formula V, which encompasses Compound 1, are "useful in the treatment of a variety of cancers," including carcinoma of the breast, colon, lung, ovary, and pancreas (Vite 8). In addition, we agree with Appellant that results demonstrating delay in tumor growth (as opposed to regression of cancer) are sufficient to demonstrate an effective cancer treatment (Reply Br. 8).

Thus, we conclude that the Declaration provides sufficient evidence of an unexpectedly superior result to overcome the Examiner's prima facie case of obviousness.

Our dissenting colleague would affirm the rejection. In her view, "it is not the Examiner's burden to show why the evidence would not be commensurate in scope with the claims" (*infra* at 11). We disagree with this reasoning. *See In re Rinehart*, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976):

> When *prima facie* obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over. Though the burden of going forward to rebut the *prima facie* case remains with the applicant, the question of whether that burden has been successfully carried requires that the entire path to decision be retraced. . . . Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself.

See also In re Piasecki, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).

Thus, as we understand the case law, when evidence is submitted to rebut a prima facie case of obviousness, the Examiner must consider anew whether the claimed invention would have been obvious in light of all the evidence of record. If the rejection is maintained, then, the Examiner must explain why the rebuttal evidence is insufficient to overcome the evidence of obviousness, including (if applicable) why the evidence is not commensurate in scope with the claims.

We also disagree with the dissent's reading of *In re Soni*. Our colleague would seemingly prefer to follow the dissenting opinion in *Soni* rather than the opinion of the court. "Dissenting opinions are often helpful in showing positions that were not adopted by the court. However, they are not the law." *Pioneer Hi-Bred Int'l Inc. v. J.E.M. Ag Supply Inc.*, 200 F.3d 1374, 1378, 53 USPQ2d 1440, 1442 (Fed. Cir. 1999). We are not free to

choose which precedents of the U.S. Court of Appeals for the Federal Circuit we will follow. Our role is to apply the law as best we understand it, and that is what we have done.

SUMMARY

When we weigh Appellant's evidence of unexpected results against the evidence supporting the prima facie case of obviousness, we conclude that the Examiner's position is not supported by the preponderance of the evidence of record. We therefore reverse the rejections of claims 117-130 under 35 U.S.C. § 103. The rejection of claims 101-111 and 113-116 were not appealed and are therefore affirmed.

REVERSED

LINCK, *Administrative Patent Judge*, dissenting.

I respectfully dissent and thus would affirm the Examiner's § 103(a) rejection of claims 117-130.

The majority finds a prima facie case of obviousness has been made (*see supra* p. 5) but then concludes Appellant's Declaration has overcome the prima facie case (*see supra* pp. 6-7), based on data for a single dosage in a single type cancer, i.e., colon cancer. (Declaration ¶¶ 10-13; *see also* Answer 10.)

I agree with the majority that the Examiner has made a prima facie case of obviousness. And, to the extent Appellant's data show the two-drug combination is *more* effective than the two drugs used separately *when added together*, that data may be sufficient to overcome the prima facie case for colon cancer at the particular dose used in the study. (*See* Declaration ¶ 14.) Such data might also support claims to a method of treating colon cancer over a modest dosage range. But the claims are not so limited. (*See, e.g.*, claim 117 (reciting seven types of cancer and very broad dosage ranges). Contrary to Appellant's argument that all claims require "a synergistic or greater than additive effect" (Reply Br. 3), they merely require, e.g., "dosage unit[s]" that will provide a greater anti-cancer effect than the effect obtainable with either the dosage unit of capecitabine or the dosage unit of Compound (1) *alone*." (Claim 117 (emphasis added).) As the Examiner found, the claimed dosage units likely cover "all dosage ranges" (Answer 10) and thus likely include ones that would not yield synergism or unexpected results.

With respect to the six types of cancers recited in the claims other than colon cancer, Appellant has not provided any evidence of *unexpected* results. According to the majority, the prior art teaches the two drugs are

"'useful in the treatment of a variety of cancers,' including carcinoma of the breast, colon, lung, ovary, and pancreas." (*Supra* p. 7.) While the prior art may contain evidence that capecitabine and Compound 1 are used in various cancers and thus provide evidence that the combination would also be useful in the same various cancers, I am not aware of any suggestion the combination would provide unexpected results, or be "synergistic," in any of these six types of cancer.

The burden is on Appellant to overcome the prima facie case with objective evidence commensurate in scope with the claims. *See, e.g., In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) ("It is well established that the objective evidence of nonobviousness must be commensurate in scope with the claims"). Once a prima facie case has been made, the burden shifts to the Appellant to overcome it with evidence commensurate in scope with the claims. Contrary to the majority's view (*supra* p. 7), at that point it is not the Examiner's burden to show why the evidence would not be commensurate in scope with the claims. In this case, the "claims . . . are much broader in scope" than Appellant's showing, and I find "'no adequate basis for reasonably concluding'" the recited broad dosages "would behave in the same manner" as the tested dosages in all the recited cancers. *In re Lindner*, 457 F.2d at 508, 173 USPQ at 358.

In reaching its conclusion that Appellant has overcome the Examiner's prima facie case, the majority relies on Appellant's statement that the experiments described in his Declaration "demonstrated a synergistic effect" that he found "surprising." (*Supra* p. 6 (quoting Declaration ¶ 15 and citing *In re Soni*, 54 F.3d 746, 751, 34 USPQ2d 1684,

1688 (Fed. Cir. 1995)).) *Soni* does not support the proposition that unsupported or conclusory statements are sufficient to overcome a prima facie case of obviousness. *See Soni*, 54 F.3d at 750, 34 USPQ2d at 1687 (quoting, e.g., *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("'Mere argument or conclusory statements . . . does not suffice.'")). In essence, the majority's broad reading of *Soni* would put into place a "new rule" that would permit an applicant to overcome a prima facie case by merely showing "'substantially improved results'" and stating that the results were "'unexpected.'" *Soni*, 54 F.3d at 755, 34 USPQ2d at 1691-92 (Michel, J., dissenting) (quoting 54 F.3d at 751, 34 USPQ2d at 1688) (the same language quoted and relied upon by the majority (*supra* p. 6)). Such a test would "eliminate[] the applicant's burden of coming forward with objective evidence of unexpectedness" and "may be inherently unworkable." *Id.*, 34 USPQ2d at 1692 (Michel, J., dissenting).

Further, in *Soni*, the issue of whether the data were commensurate in scope with the claims was raised for the first time on appeal, and the court refused to consider it. *Id.* at 751, 34 USPQ2d at 1688.

Appellant has claimed a method reciting the combination of two prior art compounds known to be useful in treating cancer for that "very same purpose." (Answer 7.) Given this situation, the majority properly found the Examiner had made a prima facie case of obviousness. The majority also properly found "there would have been a reasonable expectation that administering capecitabine in combination with Compound 1 would provide a greater anti-cancer effect than would administering either capecitabine or Compound 1 alone" (*see supra* p.5). Yet the majority decision will likely

result in a patent covering a method of using the combination of these two known chemotherapeutics, with predictable results, i.e., "a greater anti-cancer effect than would administering either capecitabine or Compound 1 alone." (*See, e.g.,* claim 117.) Issuing such a patent would take from the public's hands that which it previously possessed.

I would affirm the Examiner's rejection of claims 117-130 under § 103(a).

dm

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